Viread (tenofovir)

Viread is supplied in 300-mg tablets that are almond shaped, light blue film coated, and embossed with "GILEAD" and "4331" on one side and with "300" on the other side.

Also known as: tenofovir, tenofovir DF, tenofovir disoproxil fumarate, PMPA, and bis(POC)PMPA.

Background. Viread is an anti-HIV drug manufactured by Gilead Sciences Inc. The drug is a nucleo*tide* reverse transcriptase inhibitor, similar in action to the nucleoside reverse transcriptor inhibitor (NRTI) class of HIV drugs. The FDA approved Viread for use in fighting HIV in October 2001.

Coformulations. Truvada (a fixed-dose, once-daily, co-formulation of Viread with the HIV drug Emtriva) was approved by the FDA in August 2004. Gilead is currently working with Bristol-Myers Squibb to develop a combination pill of Sustiva, Viread, and Emtriva as a complete, one-pill, once-a-day HIV regimen.

Dose. The recommended dose of Viread is one 300 mg tablet once a day.

Food restrictions. Viread can be taken with or without food.

Storage. Viread should be stored at room temperature (77ºF).

Patient assistance. Gilead Sciences Inc. has a Reimbursement and Assistance Program for Viread. The number is 800.226.2056.

Side effects and toxicity. The most common side effects of Viread are nausea, diarrhea, weakness, vomiting, and flatulence (intestinal gas), pain, headache, and rash. Caution should be used in patients with bone disease risk factors or a history of bone problems. Bone monitoring is recommended for HIV infected patients who have a history of pathologic bone fracture or are at risk for osteopenia, as well as supplementation with calcium and vitamin D. Long-term study has shown that the lumbar spine is the most likely location for bone loss in patients taking Viread.

As with other HIV drugs, changes in body shape may occur in persons taking Viread. Changes include increased fat in the upper back and neck, breasts, and the trunk of a person's body, as well as loss of fat from the legs, arms, and face. Also, a risk of lactic acidosis and severe hepatomegaly (enlarged liver) with steatosis (fatty liver) exists with all NRTIs.

Because Viread is cleared by the kidneys, renal (kidney) impairment is a possible side effect of Viread. Persons with kidney problems must take a lower dose of Viread, to be determined by a doctor based on creatinine clearance. Viread has not been tested in persons with liver problems and is not indicated for the treatment of Hepatitis B. In fact, severe hepatitis flare-ups have been reported in HIV+ patients with Hepatitis B who stopped taking Viread. Patients should be tested for Hepatitis B before starting Viread. Pregnant women should not take Viread.

Drug interactions. Viread significantly increases the levels of Videx in your blood. This increase in Videx levels could cause an increase in Videx side effects, which may include but are not limited to pancreatitis, lactic acidosis, peripheral neuropathy, and T-cell toxicity (reduced counts of T cells). If Videx EC (the newer, "enteric-coated" formulation) and Viread are taken in the same regimen by adults (greater than 132 lbs), the dosing of Videx EC should be reduced to 250 mg, instead of the usual 400 mg. In addition, the 2 drugs should be taken together under fasting conditions or with a light meal. If buffered Videx is being used, both drugs can be taken together but under fasting conditions. **The combination of Viread and Videx may not be ideal for patients with other options; this combination should definitely not be used with Sustiva or Viramune because a greater chance of regimen failure is possible.**

Viread lowers the levels of Reyataz in the body. Therefore, boosting once-daily Reyataz (300 mg) with 100 mg of Norvir is recommended when taken with Viread (all as a single daily dose with food). Both Reyataz and Kaletra increase levels of Viread so patients taking either of these combinations should be monitored closely for Viread-related side effects.

Viread is eliminated by the kidneys and may interact with other drugs that are eliminated by the kidneys. Examples of these drugs include Zovirax (acyclovir), Valtrex (valacyclovir), Cytovene (ganciclovir), Valcyte (valgancyclovir), and Vistide (cidofovir). Company officials have stated that Viread should *definitely not* be taken with Vistide (cidofovir). Viread does not appear to have any interactions with Methadone, Hepsera (adefovir dipivoxil), or ribavirin.

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Additional info:

Resistance and cross resistance. Viread selects for the K65R mutation, the same mutation selected for by Ziagen and Videx. Patients with mutations associated with other classes of anti-HIV drugs maintained susceptibility to Viread and their viral load drops ranged from 0.04 to 1.0 log. In persons with no mutations associated with Retrovir (at codons 41, 67, 70, 210, 215,or 219; also referred to as nucleoside analog mutations or NAMs), the average viral load drop was 0.85 log. In patients with 1 or 2 NAMs, the average viral load dropped 0.6 log. In patients with 3 or more NAMs, including 41L and 210W, the viral load drop was reduced to 0.23 log. In patients with 3 or more NAMs, not including 41L or 210W, the average viral load drop was 0.65 log. In addition, this study seems to indicate that mutations emerged more slowly in patients who added Viread than persons who added placebo to their standard background therapy. Nucleoside reverse transcriptase inhibitor (NRTI) mutations occurred in 24% of patients in the placebo group versus 16% taking Viread. Similarly, non-nucleoside reverse transcriptase inhibitor (NNRTI) mutations arose in 10% of patients in the placebo arm versus 5% in the Viread group. Protease inhibitor mutations emerged in 8% of the patients in the placebo arm versus 2% in the Viread arm.

Clinical data. Approval for Viread was based primarily on 2 efficacy studies. Study 907 was a 24-week, double-blind placebo controlled multicenter study of Viread added to a stable background treatment (SBT) regimen of anti-HIV drugs in 550 treatment-experienced patients. CD4 T cell counts of patients at baseline ranged from 23 to 1385 cells/mm^3 (median 426 cells/mm^3); and plasma HIV RNA ranged from 50 to 75,900 copies/mL (median 2340 copies/mL). The mean duration of prior HIV treatment was 5.4 years. At baseline 368 patients were randomized to the Viread arm and 182 patients were randomized to the placebo arm. Through week 24, the time-weighted average change from baseline HIV RNA in the Viread arm was -0.61 log versus -0.03 log in the placebo arm; similarly, the mean change in the absolute CD4 T cell count in the Viread arm was +11 versus -5 cells/mm^3 in the placebo arm. At week 24 a total of 149 patients (40%) in the Viread arm had <400 copies/mL versus 20 patients (11%) in the placebo arm. In addition, 71 patients (19%) in the Viread arm versus 2 patients (1%) in the placebo arm had <50 copies/mL at week 24.

Data through 48-weeks are reported for Study 903, a double-blind, active-controlled multicenter study comparing Viread (300 mg once daily) given in combination with Epivir (lamivudine) + Sustiva (efavirenz) versus Zerit (stavudine) + Epivir + Sustiva in 600 antiretroviral-naïve patients. The mean baseline CD4 cell count was 279 cells/mm^3 (range 3–956) and median baseline plasma HIV-1 RNA was 77,600 copies/mL (range 417–5,130,000). Patients were stratified by baseline HIV-1 RNA and CD4 count. Forty-three percent of patients had baseline viral loads >100,000 copies/mL and 39% had CD4 cell counts <200 cells/mL. At baseline, 299 patients were placed on the Viread arm and 301 patients were placed on the Zerit arm. Achievement of plasma HIV-1 RNA concentrations of <400 copies/mL at week 48 was similar between the 2 treatment groups for the population stratified at baseline on the basis of HIV-1 RNA concentration (< or >100,000 copies/mL) and CD4 cell count (< or ≥ 200 cells/mm^3). Through 48 weeks of therapy, 79% of patients in the Viread arm had <400 copies/mL versus 82% in the Zerit arm. In addition, 76% and 79% of patients in the Viread and Zerit arms, respectively achieved HIV-1 RNA <50 copies/mL. The mean increase from baseline in CD4 cell count was 169 cells/mm^3 for the Viread arm and 167 cells/mm^3 for the Zerit arm. Six percent of patients on the Viread arm experienced virologic failure versus 4% in the Zerit arm. Through 48 weeks, 8 patients in the Viread group and 6 patients in the stavudine group experienced a new CDC Class C event.

To contact The Center for AIDS, call **713.527.8219** or toll free **888.341.1788.**

P.O. Box 66306
Houston, Texas 77266-6306

1407 Hawthorne Street
Houston, Texas 77006
E-mail: ***info@centerforaids.org***
Website: ***www.centerforaids.org***